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PATENT
1340-1-016N

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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

APPLICANT	:	ROGER NOVAK AND ELAINE I. TUOMANEN		
SERIAL NO.	:	09/305,984	EXAMINER	: L. LEE
FILED	:	MAY 5, 1999	ART UNIT	: 1645
FOR	:	NOVEL ANTIBIOTICS AND METHODS OF USING THE SAME		

Certificate of Mailing Under 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, D.C. 20231 on May 3, 2001.

Michael D. Davis, Reg. No. 39,161
(Name of Registered Rep.)

Betty Schultz 5/3/01
(Signature and Date)

TRANSMITTAL LETTER

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Dear Sir:

Appellants respectfully submit three copies of a Brief For Appellants that includes an Appendix with the pending claims and three copies of the cited references. The Appeal Brief is now due on May 19, 2001.

Appellants enclose a check in the amount of $155.00 covering the requisite Government Fee. Appellants filed a Notice of Appeal received by the Patent Office on March 19, 2001 wherein Appellants reserved the right to request an Oral Hearing. This request is reiterated herein.

The Commissiner is hereby authorized to charge any additional fees that may be required by this paper, and to credit any overpayment, to Deposit Amount No. 11-1153.

Respectfully submitted,

Michael D. Davis

MICHAEL D. DAVIS
Attorney for Applicant(s)
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Date: May 3, 2001

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#16
Linda

Patent
Attorney Docket No. 1340-1-016N

5/15/01

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re Patent Application of)
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ROGER NOVAK AND ELAINE I. TUOMANEN)
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Application No.: 09/305,984)
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Filed: May 5, 1999)
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OF USING THE SAME)

Group Art Unit: 1645
Examiner: L. LEE

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CERTIFICATE OF MAILING UNDER 37 CFR 1.8

I hereby certify that this correspondence is being deposited with the United States Postal Service as first class mail in an envelope addressed to the ASSISTANT COMMISSIONER FOR PATENTS, WASHINGTON, DC 20231 on May 3, 2001.

Michael D. Davis, Reg. No. 39,161
(Name of Registered Representative)

Betty Schultz 5/3/01
(Signature and Date)

BRIEF FOR APPELLANTS

ASSISTANT COMMISSIONER FOR PATENTS
WASHINGTON, D.C. 20231

Sir:

This appeal is from the decision of the Primary Examiner dated November 29, 2000 (Paper No. 12) rejecting Claims 34-39, 68, and 69, and to an Advisory Action dated February 12, 2001 (Paper No. 14), maintaining the rejection. The Examiner has entered the Response to the final Office Action filed on January 3, 2001. The pending claims are reproduced as an Appendix to this Brief.

Enclosed is a check in the amount of $155.00 covering the requisite Government fee, and two extra copies of this Brief are being filed herewith. Appellants filed a Notice of Appeal on March 15, 2001 wherein Appellants reserved the right to request an Oral Hearing. This request is reiterated herein.

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The Commissioner is hereby authorized to charge any additional fees that may be required by this paper, and to credit any overpayment, to Deposit Account No. 11-1153.

(1) ***Real Party in Interest***:

This Appeal is taken on behalf of The St. Jude Children's Research Hospital who has been assigned the rights to the pending Application.

(2) ***Related Appeals and Interferences***:

There are no other appeals or interferences known to the Appellant, the Appellant's legal representatives, or assignee which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

(3) ***Status of the Claims***:

Claims 34-39, 68, and 69 are pending in the application. Claims 1-33 and 40-67 have been withdrawn from consideration being subject to a restriction requirement.

(4) ***Status of Amendments***:

In response to the Final Rejection dated November 29, 2000, a Response was filed by the Appellants on January 3, 2001. It is the understanding of the Appellants that this Response was entered. Subsequently, the Examiner issued an Advisory Action dated February 12, 2001 maintaining the rejection.

(5) ***Summary of Invention***:

The present invention as defined in the claims discloses methods of identifying potential agents that are capable of inhibiting the growth of and/or killing a bacterial cell. The crucial aspect of the claimed invention relates to the use of specific test cells that have been selected to have a defective His-Asp phosphorelay pathway (*see* Page 25, lines 18-28; line 8 of Page 26 through line 1 of Page 27; Page 33, lines 22-32; and line 31 of Page 34 through line 20 of Page 35 of the original Specification). In particular claimed embodiments, the bacterial cells are also resistant to the bactericidal effects of a novel peptide having the amino acid sequence of SEQ ID NO:2 and/or are vancomycin resistant.

The purpose of the claimed methods is to identify potential drugs that can be used in conjunction with and/or as an alternative to classical antibiotics.

(6) ***Issues Presented for Review***:

ISSUE

Whether Appellants' Claims 34-39, 68, and 69 are anticipated under §102(b) by Williamson *et al.*, *J. Bacteriology* **114**:105-113 (1980).

(7) ***Groupings of Claims***:

Since there is only a single issue the Appellants consider all the claims to be within the same group.

(8) ***Arguments***:

The Examiner asserts that Claims 34-39, 68, and 69 are anticipated under §102(b) by Williamson and Thomasz, *J. Bacteriology* **114**:105-113 (1980). The Examiner asserts that the cells described by Williamson and Thomasz have an identical biological phenotype, *e.g.*, vancomycin tolerance, as the cells of the claimed methods. The Examiner also asserts that Novak *et al.*, [*Nature* **399**:590-593 (1999)] indicate that vancomycin tolerance in mutant *Streptococcus pneumoniae* is due to a defective His-Asp phosphorelay pathway and therefore, the skilled artisan would conclude that the vancomycin tolerant mutant cells of Williamson and Thomasz have a defect in their His-Asp phosphorelay pathway. The Examiner further asserts that it is the burden of the Applicants to show that the vancomycin tolerant mutant cells of Williamson and Thomasz are distinguishable from the cells employed in the claimed methodology since the U.S. Patent Office does not have the facilities for examining and comparing the cells. The Examiner therefore concludes that it must be assumed that the cells are the same.

The Applicants respectfully traverse the Examiner's rejections.

The Federal Circuit has held that:

> "[a]nticipation requires identity of the claimed process and a process of the prior art; the claimed process, including each step thereof, must have been described or embodied, either expressly or inherently, in a single reference." [*Glaverbel Société Anonyme v. Northlake Marketing & Supply Inc.*, 33 USPQ2d 1496,1498 (1995)].

In the present case, a required element of the claimed process is the use of a bacterial cell that has been selected to have a defective His-Asp phosphorelay pathway. The art cited by the Examiner, *i.e.*, Williamson and Thomasz, does not teach a bacterial cell that has been

selected to have a defective His-Asp phosphorelay pathway. Therefore, Williamson and Thomasz cannot anticipate the present invention.

The Examiner appears to agree with the Applicants' fundamental premise, but attempts to cure the deficiency in Williamson and Thomasz by equating their cells with those required for the claimed methods. Thus, the Examiner rests her entire argument on her assertion that "Novak *et al.* (1999) clearly indicate that vancomycin tolerance in mutant *Streptococcus pneumoniae* is due to the defective His-Asp phosphorelay pathway" (*see* Page 2, lines 5-6 of Paper 14, the Advisory Action). However, as indicated in our prior Responses and acknowledged by the Examiner in the Advisory Action, Novak *et al.* (1999) do not state that all vancomycin tolerant *Streptococcus pneumoniae* have a defective His-Asp phosphorelay pathway. Rather, Novak *et al.* (1999) simply demonstrate that a cell having a defective His-Asp phosphorelay pathway is vancomycin tolerant. Indeed, the instant Specification teaches that cells having a defective ABC transporter can also be vancomycin tolerant [*see e.g.,* Page 76, lines 16-23 of the instant Specification]. Importantly, in the Restriction Requirement issued by the Examiner on November 9, 1999 (Paper 4) the Examiner specifically found that methods of using such cells in analogous assays were patentably distinct from the present invention. Furthermore, Charpentier *et al.*, *Mol. Microbiol.* **37(4)**:717-726 (2000) have demonstrated that *Streptococcus pneumoniae* having a defective ClpC ATPase are vancomycin tolerant even though they do not have a defect in their His-Asp phosphorelay pathway (*see* Charpentier *et al.,* Page 720, column 2, first full paragraph, bottom two lines; ClpC ATPase is believed to be a chaperone-regulator of proteolysis and a heat-shock protein). Therefore, whereas mutant *Streptococcus pneumoniae* having a defective His-Asp phosphorelay pathway can be vancomycin tolerant, all

vancomycin tolerant *Streptococcus pneumoniae* do not have a defective His-Asp phosphorelay pathway.

The Federal Circuit has also held that:

> "To establish inherency, the extrinsic evidence 'must make clear that the missing descriptive matter is necessarily present in the thing described in the reference, and that it would be so recognized by persons of ordinary skill.' 'Inherency, however, **may not be established by probabilities or possibilities**. The **mere fact** that a certain thing **may result** from a given set of circumstances **is not sufficient**.'" [*In re Robertson* 49 USPQ2d 1949, 1950-1951 (1999), citations omitted, emphasis added.]

Whereas the present invention provides methods of using cells that specifically have a defective His-Asp phosphorelay pathway, Williamson and Thomasz only provide cells that are vancomycin tolerant. In fact, Williamson and Thomasz made no effort to determine the genotypes of their cells. Therefore, Williamson and Thomasz do not provide the requisite cells having the specified genotype for performing the claimed methods since the vancomycin tolerance phenotype can be due to any of a number of factors (including a defective ABC transporter or a defective ClpC ATPase as indicated above). Indeed, the skilled artisan could not assume that all (if any) of the cells of Williamson and Thomasz have a defective His-Asp phosphorelay pathway. Therefore, as the Federal Circuit has held, the **possibility** that the cells of Williamson and Thomasz **may have** had a defective His-Asp phosphorelay pathway **is not sufficient** to anticipate the present invention. Therefore, Williamson and Thomasz do not anticipate the claimed invention.

In view of the above and foregoing, it is respectfully requested that the Board of Patent Appeals and Interferences review and reverse the adverse decision of the Examiner regarding the above-identified Claims.

Respectfully submitted,
KLAUBER & JACKSON

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Date: May 3, 2001

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(9) **APPENDIX**

CLAIMS INVOLVED IN THE APPEAL

34. A method of identifying an agent that is capable of inhibiting the growth of or killing a bacterial cell comprising:

(a) contacting the agent with a bacterial cell, wherein the bacterial cell has been selected to have a defective His-Asp phosphorelay pathway; and

(b) determining whether the cell is killed or its growth is inhibited; wherein an agent is identified as capable of killing or inhibiting the growth of a bacterial cell if it kills or inhibits the growth of the bacterial cell.

35. The method of Claim 34 wherein the bacterial cell is a vancomycin tolerant cell.

36. The method of Claim 34 wherein the bacterial cell is not killed by a peptide having the amino acid sequence of SEQ ID NO:2.

37. The method of Claim 34 wherein the bacterial cell is a *pneumococcal* cell.

38. The method of Claim 35 wherein the His-Asp phosphorelay pathway lacks a functional sensor histidine kinase having a wild type amino acid sequence of SEQ ID NO:14.

39. The method of Claim 35 wherein the His-Asp phosphorelay pathway lacks a functional response regulator having a wild type amino acid sequence of SEQ ID NO:16.

68. The method of Claim 38 wherein the bacterial cell is not killed by a peptide having the amino acid sequence of SEQ ID NO:2.

69. The method of Claim 39 wherein the bacterial cell is not killed by a peptide having the amino acid sequence of SEQ ID NO:2.

(10) REFERENCES INCLUDED

1. Novak *et al., Nature* **399**:590-593 (1999).

2. Charpentier *et al., Mol. Microbiol.* **37(4)**:717-726 (2000).

3. Williamson *et al., J. Bacteriology* **114**:105-113 (1980).

11) LIST OF AUTHORITIES CITED

1. *Glaverbel Sociéte Anonyme v. Northlake Marketing & Supply Inc.*, 33 USPQ2d 1496 (1995).

2. *In re Robertson* 49 USPQ2d 1949 (1999).